



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>6</sup> : C12N 15/54, A61K 48/00, 38/45, 38/46, 47/42, C12Q 1/48, C12N 9/10, 9/24 // (A61K 38/45, 31:52)</p>	A3	<p>(11) International Publication Number: <b>WO 95/07718</b></p> <p>(43) International Publication Date: 23 March 1995 (23.03.95)</p>
<p>(21) International Application Number: PCT/US94/10130</p> <p>(22) International Filing Date: 14 September 1994 (14.09.94)</p> <p>(30) Priority Data: 122,321 14 September 1993 (14.09.93) US</p> <p>(71) Applicants: THE UAB RESEARCH FOUNDATION [US/US]; The University of Alabama at Birmingham, Administration Building, Suite 1120, 701 South 20th Street, Birmingham, AL 35294-0111 (US). SOUTHERN RESEARCH INSTI- TUTE [US/US]; 2000 Ninth Avenue South, Birmingham, AL 35205 (US).</p> <p>(72) Inventors: SORSCHER, Eric, J.; 1019 Thirty-Second Street South, Birmingham, AL 35205 (US). PARKER, William, B.; 1022 Thirty-Second Street South, Birmingham, AL 35202 (US). BENNETT, Leonard, L., Jr.; 3742 Montrose Road, Birmingham, AL 35213 (US).</p> <p>(74) Agents: PABST, Patrea, L. et al.; Arnall Golden &amp; Gregory, 2800 One Atlantic Place, 1201 West Peachtree Street, Atlanta, GA 30309-3400 (US).</p>		<p>(81) Designated States: CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 13 April 1995 (13.04.95)</p>
<p>(54) Title: PURINE NUCLEOSIDE PHOSPHORYLASE GENE THERAPY FOR HUMAN MALIGNANCY</p>		
<p>(57) Abstract</p>		
<p>Methods and compositions for killing replicating or non-replicating, targeted mammalian cells and bystander cells, comprising: (a) transfecting or transducing mammalian cells with a nucleic acid encoding a purine analog nucleoside cleavage enzyme, or providing the targeted cells directly with the enzyme; and (b) contacting the targeted cells with a purine analog nucleoside substrate for the enzyme to produce a toxic purine base analog thereby killing the targeted cells and bystander cells. In the present method of killing cells, the enzyme can be an <i>E. coli</i> purine analog nucleoside phosphorylase.</p>		

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 94/10130

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 6 C12N15/54 A61K48/00 A61K38/45 A61K38/46 A61K47/42  
 C12Q1/48 C12N9/10 C12N9/24 //(A61K38/45,31:52)

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 6 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 392 745 (CELLTECH LIMITED) 17 October 1990  see the whole document, and noting especially example 7 ---	1-4, 7-10, 14-16, 18-23, 26-29, 33,34, 36-39, 41-43
A	EP,A,0 415 731 (THE WELLCOME FOUNDATION LIMITED) 6 March 1991 see the whole document --- -/--	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

10 March 1995

Date of mailing of the international search report

17.03.95

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## INTERNATIONAL SEARCH REPORT

 Intern al Application No  
 PCT/US 94/10130

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, USA, vol.89, January 1992, WASHINGTON D.C., USA pages 33 - 37 MULLEN ET AL 'TRANSFER OF THE BACTERIAL GENE FOR CYTOSINE DEAMINASE TO MAMMALIAN CELLS CONFERS LETHAL SENSITIVITY TO 5-FLUOROCYTOSINE:A NEGATIVE SELECTION SYSTEM' see the whole document ---	
A	ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol.35, no.5, May 1991, WASHINGTON D.C., USA pages 851 - 857 AVERETT ET AL '6-METHOXYPURINE ARABINOSIDE AS A SELECTIVE AND POTENT INHIBITOR OF VARICELLA-ZOSTER VIRUS' see the whole document ---	
P, X	GENE THERAPY, vol.1, no.4, July 1994, BASINGSTOKE, UK pages 233 - 238 SORSCHER ET AL 'TUMOR CELL BYSTANDER KILLING IN COLONIC CARCINOMA UTILIZING THE ESCHERICHIA COLI DEOD GENE TO GENERATE TOXIC PURINES' see the whole document ---	1-47
O, P, X	PROCEEDINGS OF THE 85TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, APRIL 10-13, 1994, vol.35, March 1994, SAN FRANCISCO, CA, USA page 374 PARKER ET AL 'TUMOR CELL BYSTANDER KILLING IN COLONIC CARCINOMA UTILIZING THE E.COLI DEOD GENE PRODUCT TO GENERATE TOXIC PURINES' see abstract no.2229 -----	1-47

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 94/ 10130

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 1-17 and 19 partially as far as they relate to an in vivo method and claim 18 completely are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Intern al Application No PCT/US 94/10130
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0392745	17-10-90	AT-T- 113481	15-11-94
		AU-B- 641156	16-09-93
		AU-A- 5404290	05-11-90
		DE-D- 69013740	08-12-94
		WO-A- 9011782	18-10-90
		GB-A, B 2240921	21-08-91
		JP-T- 3505586	05-12-91
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		AU-A- 6199190	07-03-91
		AU-B- 6458794	08-09-94
		CN-A- 1050899	24-04-91
		JP-A- 3172189	25-07-91